Systems Biology: Theoretical Biology

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Spatial Patterns

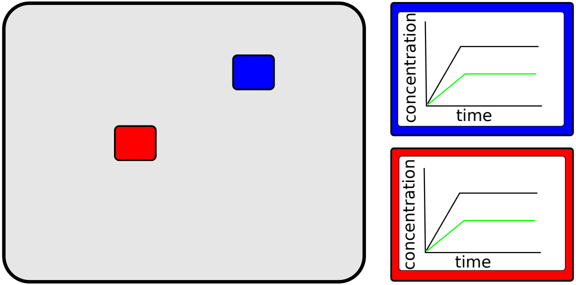
Contents

- Why space matters.
- Stationary and dynamic spatial patterns.
- Incorporating space into models:
  - Modeling diffusion with PDEs.
  - Modeling discrete space with Cellular Automata.

Incorporating space

Homogeneous situations

The same things happen at the same time everywhere.
This is the case in well-mixed systems: differences disappear rapidly!



We can describe what happens everywhere by describing the dynamics in a single point. No need to include space in a model.

Space: To ignore or not to ignore?

When modeling homogeneous systems, we can ignore space.
We can e.g. use a single system of differential equations for all points.
Examples:

- Concentrations in well-mixed solutions.
- Populations of highly mobile individuals in a relatively small, continuous area.

But, not all systems are well-mixed!
In fact, real-life biological systems are rarely homogeneous.
Examples of such heterogeneous systems:

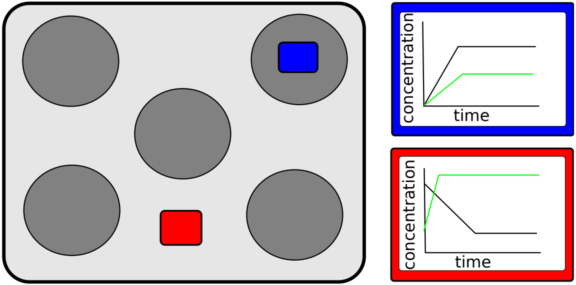
- In cells, reactions may occur on the membrane, in the cytoplasm or in an organelle.
- In large populations, individuals are more likely to mate with a neighbour than with a distant other.

Often complete mixing is of these systems is assumed in models, to make things simpler. This may or may not be a reasonable assumption.

Patterns in space

Heterogeneous situations

Different things happen at different points.
But dynamics at different points are not independent!
Between places, there may be diffusion, migration, flow, etc.



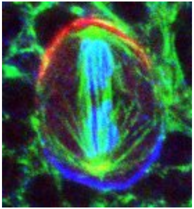
The dynamics in a single point do not describe the dynamics of the whole system. Neither do the independent dynamics in two points.
→ We need to describe the dynamics in all (different) points.
→ We need to include how local points affect each other.

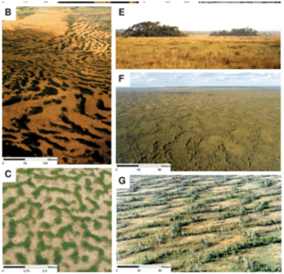
Patterns in biology: scale

Patterns occur on very different space and time-scales.

Consider for example:

- Cell polarisation.
- Skin pigmentation.
- Ecosystem patterns (soil, water, vegetation, etc.).

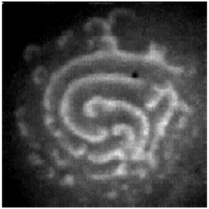




Patterns in biology: dynamics

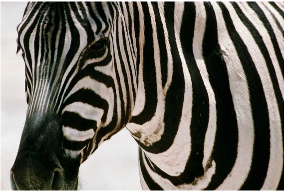
Dynamic patterns

Patterns that vary over time,
e.g. wave patterns.



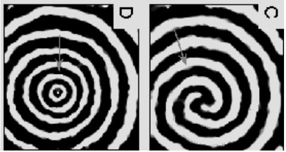
Stationary patterns

Patterns that do not change (much),
after initialisation.



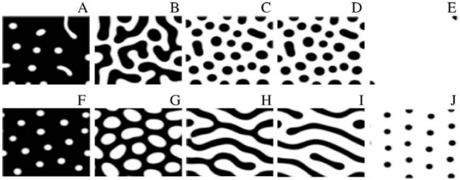
Patterns in biology: shape

Patterns can have all kinds of shapes:
Dynamic patterns are often waves or spirals



From: hopf.chem.brandeis.edu

Stationary patterns are often spots or stripes



From: Kefi *et al*, Theor. Ecology 2010

Incorporating space in models

If you're interested in spatial patterns, you'll need to include space.
To incorporate space in models we need to do two things:

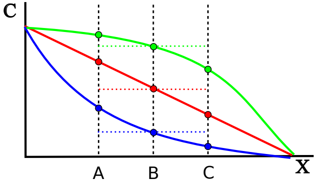
- model the dynamics in **each individual point** in space, and
- **couple** the dynamics of variables in nearby points.

Simplest spatial coupling:
Diffusion, the flow of particles from high to low concentrations.

Note that we can also use this to model diffusion-like behaviour, such as the migration of animals.

How to model diffusion

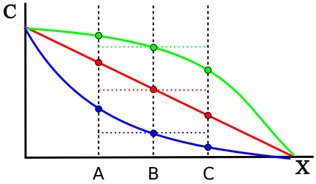
Assume a narrow 1D strip of points with a concentration gradient:



- In **all cases**, the concentration in **A** is larger than the concentration in **B**, which in turn is larger than the concentration in **C**. So in all points the flow of particles will be to the **right** $\rightarrow$.
- In the upper case the inflow concentration difference **A-B** is **smaller** than the outflow difference **B-C**. So the concentration in point **B** will **decrease** over time ($\downarrow$).
- In the lower case, the inflow concentration difference **A-B** is **larger** than the outflow difference **B-C**. So the concentration in point **B** will **increase** over time ($\uparrow$).
- In the middle case, inflow equals outflow. So the *concentration* in point **B** will **not change** over time!

How to model diffusion

Assume a narrow 1D strip of points with a concentration gradient:



- The **slope** of the concentration over distance ($\frac{\partial c}{\partial x}$, the *steepness of the concentration gradient*) will determine the **direction** of flow.
- The rate with which this slope/steepness changes over distance (the **second derivative** $\frac{\partial^2 c}{\partial x^2}$) wil determine how the concentration changes *over time* ($\frac{\partial c}{\partial t}$).

So to describe diffusion, we can write:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}$$

whereby D is a **diffusion constant** (which depends on how conductive the medium is to flow).

ODEs and PDEs

ODE: Ordinary Differential Equation

$$\frac{\mathrm{d}N}{\mathrm{d}t} = f(N)$$

We assume that N depends on time t, but not on place x.

PDE: Partial Differential Equation

$$\frac{\partial N}{\partial t} = f(N) + D\frac{\partial^2 N}{\partial x^2}$$

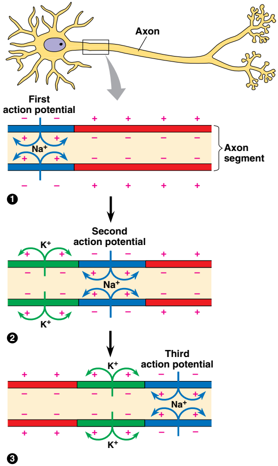
- Here, N depends on both t and x.
- The equation is applied per point in space.
- The diffusion term couples different locations.
- We can derive to either t or x, so partial rather than normal derivatives.

Example of a spatial PDE model

Modeling action potential propagation along an axon:

$$\frac{\partial V}{\partial t} = -V(V-a)(V-1) - W + D\frac{\partial^2 V}{\partial x^2}$$
$$\frac{\partial W}{\partial t} = c(V - bW)$$

We can use a simple extension of the Fitzhugh-Nagumo model.
Note that only the voltage diffuses over the axon (as only the ions diffuse).



Other types of spatial models

PDE models

- assume that variables, space and time are all **continuous**.
- This may be appropriate if numbers are high and processes are regular.

Real biological systems

- often deal with a **finite number** of **discrete** organisms/ cells/molecules.
- These occupy distinct positions, and move/replicate/etc. at distinct time points.

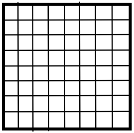
There is a suitable type of model for studying such dynamics: **Cellular Automata models** (CAs).

Other types of spatial models

Cellular Automata models (CAs) are very suitable for studying dynamics with discrete time and space.

CA model ingredients:

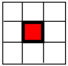
grid



variable states

□ 0 dead
■ 1 alive

neigborhood



□ neighbor
■ individual

update rules

input ind. state	sum neighbor states	output new ind. state
1	<2	0
1	2 or 3	1
1	>3	0
0	<3	0
0	3	1
0	>3	0

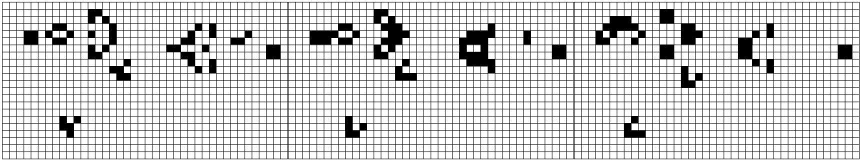
CA Example: Conway's Game of Life

Rules:

- Cell dies if less than 2 neighbours.
- Cell dies if more than 3 neighbours.
- Cell is born if exactly 3 neighbours.

update rules

input ind. state	sum neighbor states	output new ind. state
1	<2	0
1	2 or 3	1
1	>3	0
0	<3	0
0	3	1
0	>3	0



The Game of Life may not have much biological relevance.
But it does nicely illustrate how even very simple rules can lead to complex patterns!

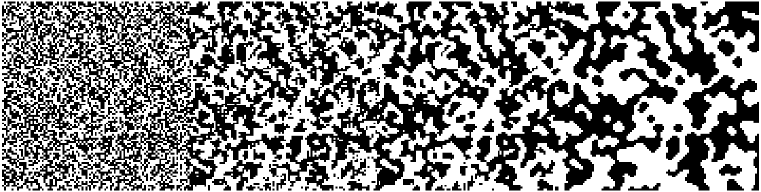
CA Example: Majority Voting

Rules:

- Start with a random grid.
- "Do what the majority around you does":
  - Cell dies if less than 4 neighbours.
  - Cell is born if more than 4 neighbours.

update rules

input ind. state	sum neighbor states	output new ind. state
1	<=3	0
1	> 3	1
0	<=4	0
0	>4	1
i.e. if sum <=4		0
i.e. if sum >4		1



These rules (a form of *positive feedback*) lead to **patch formation**.
This resembles certain vegetation pattern dynamics.

CA Example: Diffusion Limited Aggregation

Rules:

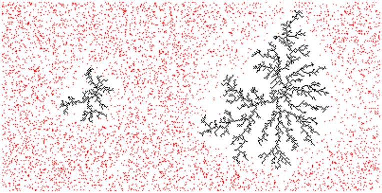
- Start with randomly moving points.
- "Freeze if one of your neighbours if frozen":
  - Stop moving if a non-moving neighbour.
  - Otherwise, move to random neighbour cell.

variable states

- 0 empty
- 1 moving
- 2 frozen

update rules

input ind. state	neighbor states	output new ind. state
0	at least one 1	0/1(random movement)
0	no 1	0
1	at least one 2	2
1	no 2	0/1 (random movement)
2	irrelevant	2



Resembles the growth of minerals, snowflakes and corals.

Summary: Types of Models

ODE models

- Equation: processes in a single location, or in a **homogeneous** (well-mixed) system.
- Separate equations needed for diversity or multiple locations.
- ODEs assume that variables and time are all **continuous**.
- Behaviour and equilibria can be analysed mathematically.
- Cannot model few individuals, or complex spatial patterns.

PDE models

- Equation: processes at points in space & interaction between points.
- PDEs assume that variables, time and space are all **continuous**.
- Can model spatial processes, often used for diffusion.
- Harder to use and analyse than ODE-models.
- Cannot model few individuals, or heterogeneous space.

Summary: Types of Models

CA models

- Describe dynamics in points on a grid, and the interaction between points.
- Computer models, with **discrete** time and space.
- No mathematical analysis, only observations.
- Can model individuals, diversity, complex rules, evolution.

Other spatial models

- Individual-based models (IBMs) with continuous space
- 3D models (PDE, CA or IBM)
- Combinations of ODEs, PDEs, CAs and/or IBMs